



January 31, 2014

LCDR Christopher Steele  
Office of Naval Research  
Code 34 – Warfighter Performance  
875 N. Randolph St.  
Arlington, VA 22203-1995

**Subject: Quarterly Performance/Technical Report of the National Marrow Donor Program<sup>®</sup>**

**Reference:** Grant Award #N00014-13-1-0039 between the Office of Naval Research and the National Marrow Donor Program

Dear LCDR. Steele:

Enclosed is subject document which provides the performance activity for each statement of work task item of the above reference for the period of October 1, 2013 to December 31, 2013.

Should you have any questions as to the scientific content of the tasks and the performance activity of this progress report, you may contact our Chief Medical Officer – Dennis L Confer, MD directly at 612-362-3425.

With this submittal of the quarterly progress report, the National Marrow Donor Program has satisfied the reporting requirements of the above reference for quarterly documentation. Other such quarterly documentation has been previously submitted under separate cover.

Please direct any questions pertaining to the cooperative agreement to my attention at 612-362-3403 or at [cabler@nmdp.org](mailto:cabler@nmdp.org).

Sincerely,

Carla Abler-Erickson, MA  
Contracts Manager

Enclosure: Quarterly Report with SF298

C: J. Kabisch – ACO (ONR-Chicago)  
Dr. Robert J. Hartzman, CAPT, MC, USN (Ret)  
Jennifer Ng, PhD – C.W. Bill Young Marrow Donor Recruitment and Research Program  
J. Rike - DTIC (Ste 0944)  
NRL (Code 5227)  
Dennis Confer, MD, Chief Medical Officer, NMDP  
Stephen Spellman

<b>REPORT DOCUMENTATION PAGE</b>			<b>Form Approved</b> <b>OMB No. 0704-0188</b>	
<small>Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Service, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188) Washington, DC 20503.</small>				
<b>PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.</b>				
<b>1. REPORT DATE (DD-MM-YYYY)</b> 31-01-2014		<b>2. REPORT TYPE</b> Quarterly		<b>3. DATES COVERED (From - To)</b> Oct 2013 - Dec 2013
<b>4. TITLE AND SUBTITLE</b> Development of Medical Technology for Contingency Response to Marrow Toxic Agents - Quarterly Performance/Technical Report for October 01, 2013 to December 31, 2013 Period 4			<b>5a. CONTRACT NUMBER</b> N/A	
			<b>5b. GRANT NUMBER</b> N00014-13-1-0039	
			<b>5c. PROGRAM ELEMENT NUMBER</b> N/A	
<b>6. AUTHOR(S)</b> Spellman, Stephen			<b>5d. PROJECT NUMBER</b> N/A	
			<b>5e. TASK NUMBER</b> Project 1, 2, 3, 4	
			<b>5f. WORK UNIT NUMBER</b> N/A	
<b>7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)</b> National Marrow Donor Program 3001 Broadway St., N.E., Ste. 500 Minneapolis, MN 55413			<b>8. PERFORMING ORGANIZATION REPORT NUMBER</b> N/A	
<b>9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)</b> Office of Naval Research 875 N. Randolph St. Arlington, VA 22203			<b>10. SPONSOR/MONITOR'S ACRONYM(S)</b> ONR	
			<b>11. SPONSORING/MONITORING AGENCY REPORT NUMBER</b> N/A	
<b>12. DISTRIBUTION AVAILABILITY STATEMENT</b> Approved for public release; distribution is unlimited				
<b>13. SUPPLEMENTARY NOTES</b> N/A				
<b>14. ABSTRACT</b> <u>1. Contingency Preparedness:</u> Collect information from transplant centers, build awareness of the Transplant Center Contingency Planning Committee and educate the transplant community about the critical importance of establishing a nationwide contingency response plan.  <u>2. Rapid Identification of Matched Donors :</u> Increase operational efficiencies that accelerate the search process and increase patient access are key to preparedness in a contingency event.  <u>3. Immunogenetic Studies:</u> Increase understanding of the immunologic factors important in HSC transplantation.  <u>4. Clinical Research in Transplantation:</u> Create a platform that facilitates multicenter collaboration and data management.				
<b>15. SUBJECT TERMS</b> Research in HLA Typing, Hematopoietic Stem Cell Transplantation and Clinical Studies to Improve Outcomes				
<b>16. SECURITY CLASSIFICATION OF:</b>		<b>17. LIMITATION OF ABSTRACT</b> Same as Report	<b>18. NUMBER OF PAGES</b> 20	<b>19a. NAME OF RESPONSIBLE PERSON</b> Dennis L. Confer, MD – Chief Medical Office
<b>a. REPORT</b> U	<b>b. ABSTRACT</b> U			<b>c. THIS PAGE</b> U

Grant Award N00014-13-1-0039

DEVELOPMENT OF MEDICAL TECHNOLOGY  
FOR CONTINGENCY RESPONSE TO MARROW TOXIC AGENTS  
QUARTERLY  
PERFORMANCE / TECHNICAL REPORT  
FOR  
OCTOBER 01, 2013 to DECEMBER31, 2013  
PERIOD 4

Office of Naval Research

And

The National Marrow Donor Program  
3001 Broadway Street N.E.  
Minneapolis, MN 55413  
1-800-526-7809

**QUARTER PROGRESS REPORT****Development of Medical Technology for Contingency Response to Marrow Toxic Agents****October 01, 2013 through December 31, 2013**

<b>TABLE OF CONTENTS</b>			
<b>TASK</b>	<b>DESCRIPTION</b>	<b>STATUS</b>	<b>PAGE</b>
<b>IIA</b>	<b>Contingency Preparedness</b>		
<b>IIA.1</b>	<b>Objective 1 – Care Plans by Transplant Physicians</b>		
	Task 1 – Secure Interest of Transplant Physicians	Open	4
	Task 2 – GCSF in Radiation Exposure	Closed	5
	Task 3 – Patient Assessment Guidelines	Closed	5
	Task 4 – National Data Collection and Management Model	Closed	5
<b>IIA.2</b>	<b>Objective 2 – Coordination of Care of Casualties</b>		
	Task 1 – Contingency Response Network	Open	5
	Task 2 – Standard Operating Procedures	Closed	5
<b>IIA.3</b>	<b>Objective 3 – Information Technology Infrastructure</b>		
	Task 1 – Disaster Recovery	Closed	5
	Task 2 – Critical Facility and Staff Related Functions	Closed	5
<b>II.B</b>	<b>Rapid Identification of Matched Donors</b>		
<b>II.B.1</b>	<b>Objective 1 – Resolution of Speeds Donor Selection</b>		
	Task 1 – Increase Registry Diversity	Open	6
	Task 2 – Evaluate HLA-DRB1 High Resolution Typing	Closed	6
	Task 3 – Evaluate HLA-C Typing of Donors	Closed	6
	Task 4 – Evaluate Buccal Swabs	Open	7
	Task 5 – Enhancing HLA Data for Selected Donors	Closed	8
	Task 6 – Maintain a Quality Control Program	No Activity	8
<b>II.B.2</b>	<b>Objective 2 – Improve HLA Quality &amp; Resolution</b>		
	Task 1 – Collection of Primary Data	No Activity	8
	Task 2 – Validation of Logic of Primary Data	Closed	8
	Task 3 – Reinterpretation of Primary Data	Closed	9
	Task 4 – Genotype Lists & Matching Algorithm	No Activity	9
<b>II.B.3</b>	<b>Objective 3 – Algorithm to Predict Best Donor</b>		
	Task 1 – Incorporate Frequencies into Matching Algorithm	No Activity	9
	Task 2 – Enhancement of EM Algorithm	No Activity	9
	Task 3 – Optimal Registry Size Analysis	No Activity	9
	Task 4 – Target Underrepresented Phenotypes	No Activity	9

**QUARTER PROGRESS REPORT****Development of Medical Technology for Contingency Response to Marrow Toxic Agents****October 01, 2013 through December 31, 2013**

	Task 5 – Bioinformatics Web Site	No Activity	10
	Task 6 – Utilize Search Strategy Advisors to Improve Algorithm	No Activity	10
	Task 7 – Population Genetics	Closed	10
	Task 8 – Haplotype Matching	Closed	10
	Task 9 – Global Haplotype/Benchmark	Closed	10
<b>IIB.4</b>	<b>Objective 4 – Reduction of Donor Matching Time</b>		
	Task 1 – Expand Network Communications	Closed	10
	Task 2 – Central Contingency Management	Open	10
	Task 3 – Benchmarking Analysis	Closed	11
	Task 4 – Expand Capabilities of Collection and Apheresis Centers	Closed	11
<b>IIC.</b>	<b>Immunogenetic Studies</b>		
<b>IIC.1</b>	<b>Objective 1 – Influence of HLA Mismatches</b>		
	Task 1 – Donor Recipient Pair Project	Open	11
<b>IIC.2</b>	<b>Objective 2 – Role of Other Loci and GVHD</b>		
	Task 1 – Analysis of Non-HLA Loci	No Activity	13
	Task 2 – Related Pairs Research Repository	Closed	13
	Task 3 – CIBMTR Integration	Closed	13
<b>IID</b>	<b>Clinical Research in Transplantation</b>		
<b>IID.1</b>	<b>Objective 1 – Clinical Research Improves Outcomes</b>		
	Task 1 – Observational Research, Clinical Trials and NIH Transplant Center	Open	13
	Task 2 – Research with NMDP Donors	Closed	14
	Task 3 – Expand Immunobiology Research	Open	14
	Acronym List		17

## QUARTER PROGRESS REPORT

## Development of Medical Technology for Contingency Response to Marrow Toxic Agents

October 01, 2013 through December 31, 2013

**IIA. Contingency Preparedness – Objective 1:** Recovery of casualties with significant myelosuppression following radiation or chemical exposure is optimal when care plans are designed and implemented by transplant physicians

**IIA.1 Task 1:** *Maintain the Radiation Injury Treatment Network (RITN) to prepare for the care of patients resulting from a hematopoietic toxic event.*

**Period 1 Activity:**

- 98% (54 of 55) RITN hospitals completed all of their tasks on time, four requested an extension and three were inactive due to competing priorities (e.g. HIS implementation, staff turnover or FACT Accreditation)
- RITN Medical Advisor activity; Dr. Weinstock participated in the following activities supporting the Radiation Injury Treatment Network:
  - He provided feedback for the new Acute Radiation Syndrome Interactive Management Tool for the Radiation Emergency Medical Management website supported by the National Library of Medicine
  - He participated in the organization and editing of grant requests to BARDA for funding to support a G-CSF user managed inventory program through an interagency agreement with the Office of Naval Research.
  - He worked with representatives of the Department of Health and Human Services to pursue funding for a G-CSF user managed inventory program through the Hospital Preparedness Program
  - He assisted with the 2014 RITN tabletop exercise
  - He helped develop the Dana-Faber/Brigham and Women's radiation emergency drill for 2014
  - He provided guidance to commercial entities with interest in developing radiation countermeasures
  - He assisted with the recruitment of new RITN centers
  - He co-authored the chapter on Nuclear and Radiological Events in KOENIG & SCHULTZ: Disaster Medicine, 2nd Edition
- Conducted two monthly RITN Center conference calls to review task completion status and allow a venue for centers to talk to peers
- Conducted a webinar entitled "RITN Year in Review" to present the accomplishments during 2013 and the goals for 2014

**QUARTER PROGRESS REPORT****Development of Medical Technology for Contingency Response to Marrow Toxic Agents****October 01, 2013 through December 31, 2013***IIA.1 Task 2: GCSF in Radiation Exposure – This task is closed.**IIA.1 Task 3: Patient Assessment Guidelines and System Enhancements – This task is closed**IIA.1 Task 4: National Data Collection Model – This task is closed.***IIA. Contingency Preparedness – Objective 2:** Coordination of the care of casualties who will require hematopoietic support will be essential in a contingency situation.*IIA.2 Task 1: Ensure NMDP maintains effective plans to continue critical facility and staff-related functions as a result of operations interruption events.***Period 1 Activity:**

- Successfully conducted two exercises to test the ability of Repository staff to complete KitMaker operations from alternate locations in the event that the Repository building was not habitable; the first exercise was conducted at the Coordinating Center and for the second exercise the KitMaker activity was redirected to the Department of Defense Donor Center.

*IIA.2 Task 2: Sibling Typing Standard Operating Procedures – This task is closed***IIA. Contingency Preparedness – Objective 3:** NMDP's critical information technology infrastructure must remain operational during contingency situations that directly affect the Coordinating Center.*IIA.3 Task 1: I.S. Disaster Recovery – This task is closed.**IIA.3 Task 2: Critical Facility and Staff Related Functions – This task is closed.*

## QUARTER PROGRESS REPORT

### Development of Medical Technology for Contingency Response to Marrow Toxic Agents

October 01, 2013 through December 31, 2013

**IIB. Rapid Identification of Matched Donors – Objective 1:** Increasing the resolution and quality of the HLA testing of volunteers on the registry will speed donor selection.

***IIB.1 Task 1:*** *Expand the genetic diversity of the Registry through continued addition of adult donors and cord blood units, utilizing high volume HLA typing methodologies.*

**Period 4 Activity:**

**2-Step Activation at Live Drive Registration:**

- The 2-Step Activation Phase Two Pilot ran from March 28 through August 28, 2013. Phase Two included an online activation channel, in addition to the Phase One channels of phone and text activation.
- In Phase Two, 3954 individuals participated in live drive registration through the 2-Step Activation process. Key findings of the study include:
  - Phase 2 activation rate of 48% is improved over Phase 1 rate of 43%
  - Members chose the online activation method most often (32%), followed by text-in (29%). Other methods included call-in at 15% and manual activation methods 23%.
  - Only 2% of non-activators elected to activate after additional follow-up.
  - A high percentage of activators (39%) completed a follow-up online survey, indicating a high degree of engagement.
- Additional analysis is in progress.

***IIB.1 Task 2:*** *Evaluate HLA-DRB1 High Res typing – This task is closed.*

***IIB.1 Task 3:*** *Evaluate HLA-C Typing of Donors – This task is closed*

## QUARTER PROGRESS REPORT

## Development of Medical Technology for Contingency Response to Marrow Toxic Agents

October 01, 2013 through December 31, 2013

***IIB.1 Task 4:*** Evaluate the suitability of buccal swabs as a method to collect DNA samples to HLA type casualties and potential related donors in contingency situations, and to obtain research samples.

**Period 4 Activity:****Sample Storage Research Study**

- The purpose of this 5 year research study was to evaluate, over time, the quality and quantity of the DNA derived from three stored sample types: frozen whole blood, room temperature whole blood spotted on filter paper (FP) and room temperature buccal swabs (SW). This study evaluated the ability of the testing laboratories to accurately and consistently obtain HLA typing results from each stored sample type. The scientific data collected from this study has allowed the NMDP to determine the length of time samples are able to be stored and still be useful for HLA testing. All samples were tested annually.
- **Results:** Sequence Specific Oligonucleotide (SSO) and Sequence Based Typing (SBT) HLA results were accurate at all loci through the 4 year Time Point (TP). At 5 year TP, SSO results were 100% accurate, whereas SBT results were 99.4% accurate for FP and 97.3% for SWs. One FP and 4 SWs had amplification failure, 5 SWs had one allele drop-out and 1 SW had both alleles drop out. 19 FP and SW samples required repeat testing at multiple loci to obtain accurate HLA results. Sufficient DNA for HLA testing was extracted from all samples at all time points. DNA quality from frozen whole blood remained high through year 5. DNA quality consistently decreased for the FP starting at the 3 year TP, and at the 1 year TP for SWs. At the 5 year TP, 33% (10/30) of the buccal swab samples could not be successfully typed at one or more loci.
- **Conclusion:** Room temp storage of SWs and FP allows for DNA degradation, creating HLA testing inaccuracies and inefficiencies. Specifically, shorter amplicons were required to achieve accurate SBT results, which required a modification to the standard SBT reagents. DNA degradation did not affect SSO typing. Buccal swabs are a cost effective and efficient mechanism for registry DNA sample collection and storage, but shelf-life at room temperature is limited for Sanger SBT HLA typing methodology.
- **Presentation:** Results of the study were presented at the Annual ASHI Meeting held in Chicago, Illinois, in November 2013. The abstract was selected for an oral presentation, and was awarded the Best Stem Cell Case Study.

**Frozen Buccal Swab Study:**

- The study will compare swabs stored at room temperature and -30°C, for quality of DNA, quantity of DNA, and high

# **QUARTER PROGRESS REPORT**

## **Development of Medical Technology for Contingency Response to Marrow Toxic Agents**

**October 01, 2013 through December 31, 2013**

resolution HLA characterization, at selected time points over multiple years.

- IRB approval of the study is complete, volunteer QC donors have enrolled, and sample collection is underway.

***IIB 1 Task 5: Evaluate the factors of donor utilization and speed of search process after strategic upgrading of selected adult volunteer donors.***

### **Period 4 Activity:**

- No activity this period

***IIB 1 Task 6: Maintain a comprehensive quality control program.***

### **Period 4 Activity:**

Maintain a Comprehensive QC Program:

- During this quarter, the 19 cell lines that were received from the cell processing laboratory last quarter were confirmatory typed by high resolution SBT at HLA-A, B, C, DRB1, DQB1, DPB1, DQA1, and DPA1 to ensure accuracy, prior to adding the new lots to active circulation.
- In addition, 22 research cord blood units were acquired for expansion of the NMDP Cord QC Program. These units were preferentially selected based on available HLA, increasing the allelic diversity of the current cord QC inventory at a minimum by 8 unique A alleles, 17 unique B alleles, 1 unique C allele and 6 unique DRB1 alleles. In addition, acquisition of these units increased the current cord QC inventory by 45%, and provides the framework for the eventual implementation of a blind cord QC program.

**IIB. Rapid Identification of Matched Donors – Objective 2:** Primary DNA typing data can be used within the registry to improve the quality and resolution of volunteer donor HLA assignments.

***IIB 2 Task 1: Ongoing collection of primary data for validation and storage in the Registry database.***

### **Period 4 Activity:**

- No activity this period

***IIB 2 Task 2: Validation of Logic of Primary Data – This task is closed.***

# **QUARTER PROGRESS REPORT**

**Development of Medical Technology for Contingency Response to Marrow Toxic Agents**

**October 01, 2013 through December 31, 2013**

***IIB 2 Task 3: Reinterpretation of Primary Data – This Task has been merged with Task IIB2.4.***

***IIB 2 Task 4: Interpretation of the primary data into genotype lists and integration into matching algorithm to optimize placement of donors onto patient searches.***

**Period 4 Activity:**

- No activity this period

**IIB. Rapid Identification of Matched Donors – Objective 3:** Registry data on HLA allele and haplotype frequencies and on the nuances of HLA typing can be used to design computer algorithms to predict the best matched donor.

***IIB.3 Task 1: Incorporate HLA allele and haplotype frequencies into matching algorithm.***

**Period 4 Activity:**

- No activity this period

***IIB 3 Task 2: Continue to enhance the allele and haplotype frequency data to include additional loci and increased resolution for ethnic groups with input from consultants with expertise in population genetics.***

**Period 4 Activity:**

- No activity this period.

***IIB 3 Task 3: Cord Blood and Adult Donor Matching Benchmarks and Registry Modeling.***

**Period 4 Activity:**

- No activity this period.

***IIB 3 Task 4: Couple haplotype prediction methodology with donor demographic data to target recruitment to areas populated by individuals with underrepresented HLA phenotypes.***

**Period 4 Activity:**

- No activity this period.

# QUARTER PROGRESS REPORT

## Development of Medical Technology for Contingency Response to Marrow Toxic Agents

October 01, 2013 through December 31, 2013

***IIB 3 Task 5: Develop a bioinformatics web site for frequency information.***

**Period 4 Activity:**

- No activity this period.

***IIB 3 Task 6: Use NMDP's expert Search Strategy Advisors as resources to further improve the matching algorithm and donor/cord blood identification software applications with the goal to maximize the ability of the software to identify the best donors/cords for each patient.***

**Period 4 Activity:**

- No activity this period.

***IIB 3 Task 7: Population Genetics – This task was merged with Task IIB3.2***

***IIB 3 Task 8: Haplotype Matching – This task was merged with Task IIB3.2***

***IIB 3 Task 9: Global Haplotype/Benchmark – This task was merged with Task IIB3.3***

**IIB. Rapid Identification of Matched Donors – Objective 4:** Reducing the time and effort required to identify closely matched donors for patients in urgent need of HSC transplants will improve access to transplantation and patient survival in the context of a contingency response and routine patient care.

***IIB.4 Task 1: Expand Network Communications – This task is closed.***

***IIB.4 Task 2: Conduct a study of random patient search simulations to test the efficacy of centralized contingency management.***

**Period 4 Activity:**

- NMDP provided support for donor/cord blood unit identification, selection and collection for the NIH intramural unrelated donor transplant program. Activity in the last quarter was as follows:
  - 2 PBSC and 2 Cord Blood Unit collections
- CIBMTR provided support for the rapid identification of potential donors for newly diagnosed AML patients under the following clinical trial protocol:

**QUARTER PROGRESS REPORT****Development of Medical Technology for Contingency Response to Marrow Toxic Agents****October 01, 2013 through December 31, 2013**

- S1203: A Randomized Phase III Study of Standard Cytarabine plus Daunorubicin (7+3) Therapy or Idarubicin with High Dose Cytarabine (IA) versus IA with Vorinostat (IA+V) in Younger Patients with Previously Untreated Acute Myeloid Leukemia (AML)
- CIBMTR provided study-specific sample collection kits for patients, processed samples, arranged HLA typing, and generated preliminary search strategy reports to assist in the identification of donors and/or CBU through the NMDP.
- It is anticipated that 750 patients will be accrued in less than 5 years with 40% needing HLA testing and search strategy results. The trial opened in April 2013. Activity during the current quarter:
  - 69 patients enrolled in the study and 68 kits have been sent to patients
    - 60 kits were collected and returned to the repository
  - 18 patients were considered high-risk or unknown risk
    - 18 patients have been HLA typed and had a preliminary search completed.

***IIB.4 Task 3: Benchmarking Analysis – This task is closed******IIB.4 Task 4: Expand Capabilities of Collection and Apheresis Centers – This task is closed.***

**IIC. Immunogenetic Studies – Objective 1:** HLA mismatches may differ in their impact on transplant outcome, therefore, it is important to identify and quantify the influence of specific HLA mismatches. In contingency situations it will not be possible to delay transplant until a perfectly matched donor can be found.

***IIC.1 Task 1:*** Continue to evaluate HLA disparity and impact on HSC transplantation by adding selected pairs to the Donor/Recipient Pair project utilizing sample selection criteria that optimize the new data generated by the typing project.

**Period 4 Activity:****Donor Recipient Pair Project**

In 1994 a retrospective D/R Pair HLA typing project to characterize class I and class II alleles of donor/recipient paired samples from NMDP's Repository was initiated. The goals of this ongoing research project are to assay the impact of DNA-based HLA matching on unrelated donor transplant outcome, develop strategies for optimal HLA matching, evaluate the impact of matching at alternative HLA loci on transplant outcome and finally to promote the development of DNA-based high resolution HLA typing

**QUARTER PROGRESS REPORT****Development of Medical Technology for Contingency Response to Marrow Toxic Agents****October 01, 2013 through December 31, 2013**

methodologies. Presence/absence typing of 16 Killer Immunoglobulin-Like Receptor (KIR) loci (2DL1-5, 2DS1-5, 3DL1-3, 3DS1, 2DP1 and 3DP1) has been included.

- Auditing of SG30 KIR and SG31 HLA and KIR continued.
- SG 32 consisting of 402 single cord blood transplants, 299 double cord blood transplants and 843 donor/recipient transplants period of performance came to a close on September 30, 2013.
- HLA data loading into the data base continued this quarter and KIR data loading began and will continue into next quarter.
- Pseudo gene (KIR\*2DP1 and KIR\*3DP1) typing data not initially reported with previous KIR typings has been collected and was loaded this quarter.

Most clinical association studies of KIR have analyzed at presence/absence resolution for each gene. Although the region has long been known to be both allelically and structurally diverse, the extent of copy number variation (CNV) has only started to be clarified. CNV data has the potential to improve, association studies by reducing confounding factors and increasing haplotypic resolution.

- Analysis of the full KIR genotyped samples with CNV assignments is still ongoing.
  - Selection of future samples for CNV typing has included all haplotype variants. Determination of minority samples for inclusion is ongoing.

Current HLA matching guidelines for unrelated HCT recommend avoidance of mismatches within the Antigen Binding Domain (ABD). This recommendation is based on the hypothesis that amino acid differences outside the ABD are not immunogenic. The ABD allo-reactivity assessment project aims to provide insight impact of mismatching outside of the ABD.

- Four DRB1\*14:01:01/14:54 containing haplotypes were identified and 334 samples were typed at A, B, C, DRB1/3/4/5, DQB1 and DPB1.
- Analysis of the high resolution typings is ongoing.

**QUARTER PROGRESS REPORT****Development of Medical Technology for Contingency Response to Marrow Toxic Agents****October 01, 2013 through December 31, 2013**

**IIC. Immunogenetic Studies – Objective 2:** Even when patient and donor are HLA matched, GVHD occurs so other loci may play a role.

***IIC.2 Task 1:** Continue to develop typing protocols for non-HLA immunogenetic loci, development of a lab network, enhancement of database to capture non-HLA data and continue analyses to evaluate genetic diversity in the transplant population.*

**Period 4 Activity:**

- No activity this period.

***IIC 2 Task 2:** Related Pairs Research Repository – This task is closed.*

***IIC 2 Task 3:** CIBMTR Integration – This task is closed.*

**IID. Clinical Research in Transplantation – Objective 1:** Clinical research in transplantation improves transplant outcomes and supports preparedness for a contingency response.

***IID.1 Task 1:** Conduct observational research and interventional clinical trials.*

**Period 4 Activity:****Cord Blood Research Subcommittee**

Work continued on a study to assess CBU characteristics (viability, TNC, CFU and CD34) pre-freeze and post thaw.

- The study protocol and data collection forms were finalized and distributed.
- Participation agreements were finalized with the study cord blood banks.
- The study population was finalized and will include 944 cases of single CBU transplants. The cases for each cord blood bank were listed and distributed to the respective cord blood bank.
- Data submission was completed by all but one study cord blood bank.
- Data analysis will be conducted during the next quarter.

## QUARTER PROGRESS REPORT

### Development of Medical Technology for Contingency Response to Marrow Toxic Agents

**October 01, 2013 through December 31, 2013**

In the NMDP/Eurocord NIMA match case study it was shown that NIMA matches are associated with more common HLA types and therefore more common haplotypes. More common haplotypes may lead to better allele level matching and matching at HLA-C. Work was initiated and continued on a NIMA assessment of high resolution match grades at HLA-A, B, C, and DRB1 between transplant recipients and the cord blood unit to determine whether the NIMA phenomena may be a consequence of better allele level matching in the NIMA matched group.

- High resolution typing was imputed for loci with intermediate or low resolution typing. Typing ambiguity scores were included to determine the confidence of the imputations.
- High resolution match grades were then determined between the recipient and the cord blood unit.
- Analysis of the data will be conducted during the next quarter.

***IID.1 Task 2: Research with NMDP Donors – This task was merged with IID1.1.***

***IID.1 Task 3:***

*Expand support for immunobiology research, statistical genetics and clinical research studies under CIBMTR Immunobiology Working Committee.*

**Period 4 Activity:**

The CIBMTR IBWC met monthly during the quarter to discuss progress on ongoing research studies.

- Three abstracts were submitted and accepted for presentation:
  - Joseph Pidala, et al., *HLA-mismatch is associated with worse outcomes after myeloablative conditioning and unrelated donor hematopoietic cell transplantation: A CIBMTR analysis.* BMT Tandem 2014 annual meeting, accepted for oral presentation and chosen to receive a Best Abstracts Award.
  - Shahinaz Gadalla, et al., *Donor telomere length predicts recipient survival after allogeneic hematopoietic cell transplantation in patients with bone marrow failure syndromes.* BMT Tandem 2014 annual meeting, accepted for oral presentation.
  - Hideki Nakasone, et al., *Sensitization to HY-antigen in female donors was not associated with the post-transplant HY-IgG development nor clinical outcomes in sex-mismatched transplantation.* BMT Tandem 2014 annual meeting,

## QUARTER PROGRESS REPORT

## Development of Medical Technology for Contingency Response to Marrow Toxic Agents

October 01, 2013 through December 31, 2013

accepted for oral presentation.

- Six abstracts were presented at the ASH annual meeting:
  - Sarah Cooley, et al., *Recipient HLA-C1 enhances the clinical advantage of killer-cell immunoglobulin-like receptor B haplotype donors in myeloablative unrelated transplantation for acute Myelogenous leukemia*. ASH 2013 annual meeting, oral presentation.
  - John Koreth, et al., *HLA-mismatch is associated with worse outcomes after unrelated donor reduced intensity conditioning hematopoietic cell transplantation: A CIBMTR Analysis*. ASH 2013 annual meeting, oral presentation.
  - Salyka Sengsayadeth, et al., *Cytotoxic T lymphocyte antigen 4 (CTLA4) single nucleotide polymorphisms do not impact outcomes after unrelated donor transplant: A CIBMTR Analysis*. ASH 2013 annual meeting, oral presentation.
  - Michelle Gleason, et al., *A novel CD16xCD33 bispecific killer cell engager (BiKE) mediates a double hit for natural killer (NK) cells to target DC33+ myelodysplastic syndrome (MDS) cells and myeloid derived suppressor cells (MDSC) at all disease stages*. ASH 2013 annual meeting, oral presentation.
  - Ronald Sobecks, et al., *Influence of killer immunoglobulin-like receptor (KIR) and HLA genotypes on outcomes after reduced-intensity conditioning allogeneic hematopoietic stem cell transplantation for patients with AML and MDS: A report from the CIBMTR Immunobiology Working Committee*. ASH 2013 annual meeting, oral presentation.
  - Payal Khincha, et al., *Evaluating the utility of telomere length measurement by qPCR as a diagnostic test for dyskeratosis congenital*. ASH 2013 annual meeting, poster presentation.
- Three manuscripts were submitted:
  - Katharina Fleischhauer, et al., *Risk-associations between HLA-DPB1 T cell epitope matching and outcome of unrelated hematopoietic cell transplantation are independent from HLA-DPA1*. Submitted to BMT
  - Marcelo Fernandez-Vina, et al., *Identification of a permissible HLA mismatch in hematopoietic stem cell transplantation*. Submitted to Blood.
  - Alan Howard, et al., *Evaluation of peripheral blood stem cell quality in products transported by traditional courier or commercial overnight shipping services*. Submitted to Transfusion.

**QUARTER PROGRESS REPORT**

**Development of Medical Technology for Contingency Response to Marrow Toxic Agents**

**October 01, 2013 through December 31, 2013**

- One manuscript was published:
  - Mary Eapen, et al., *Impact of allele-level HLA matching on outcomes after myeloablative single unit umbilical cord blood transplantation for hematologic malignancy*. Blood, Oct. 18, 2013, Epub ahead of print

**QUARTER PROGRESS REPORT****Development of Medical Technology for Contingency Response to Marrow Toxic Agents****October 01, 2013 through December 31, 2013****ACRONYM LIST**

AABB	American Association of Blood Banks	HML	Histoimmunogenetics Mark-up Language
AFA	African American	HR	High Resolution
AGNIS	A Growable Network Information System	HRSA	Health Resources and Services Administration
ABD	Antigen Binding Domain	HSC	Hematopoietic Stem Cell
AML	Acute Myelogenous Leukemia	IBWC	Immunobiology Working Committee
API	Asian Pacific Islander	ICRHER	International Consortium for Research on Health Effects of Radiation
AQP	Ancestry Questionnaire Project	IDM	Infectious Disease Markers
ARS	Acute Radiation Syndrome (also known as Acute Radiation Sickness)	IHWG	International Histocompatibility Working Group
ASBMT	American Society for Blood and Marrow Transplantation	IPR	Immunobiology Project Results
ASHI	American Society for Histocompatibility and Immunogenetics	IND	Investigational New Drug
ASTHO	Association of State and Territorial Health Officials	IS	Information Services
B-LCLs	B-Lymphoblastoid Cell Lines	IT	Information Technology
BARDA	Biomedical Advanced Research and Development Authority	IRB	Institutional Review Board
BBMT	Biology of Blood and Marrow Transplant	JCAHO	Joint Commission on Accreditation of Healthcare Organizations
BCP	Business Continuity Plan	KIR	Killer Immunoglobulin-like Receptor
BCPeX	Business Continuity Plan Exercise	MDACC	MD Anderson Cancer Center
BMCC	Bone Marrow Coordinating Center	MDS	Myelodysplastic Syndrome
BMDW	Bone Marrow Donors Worldwide	MHC	Major Histocompatibility Complex
BMT	Bone Marrow Transplantation	MICA	MHC Class I-Like Molecule, Chain A
BMT CTN	Blood and Marrow Transplant - Clinical Trials Network	MICB	MHC Class I-Like Molecule, Chain B
BODI	Business Objects Data Integrator	MKE	Milwaukee
BRT	Basic Radiation Training	MRD	Minimal Residual Disease

**QUARTER PROGRESS REPORT****Development of Medical Technology for Contingency Response to Marrow Toxic Agents****October 01, 2013 through December 31, 2013**

C&A	Certification and Accreditation	MSKCC	Memorial Sloan-Kettering Cancer Center
CAU	Caucasian	MSP	Minneapolis
CBMTG	Canadian Blood and Marrow Transplant Group	MUD	Matched Unrelated Donor
CBB	Cord Blood Bank	NAC	Nuclear Accident Committee
CBC	Congressional Black Caucus	NACCHO	National Association of County & City Health Officials
CBS	Canadian Blood Service	NCBI	National Center for Biotechnology Information
CBU	Cord Blood Unit	NCBM	National Conference of Black Mayors
CDA	Clinical Document Architecture	NARR	National Alliance for Radiation Readiness
CFU	Colony Forming Unit	NCI	National Cancer Institute
CHORI	Children's Hospital of Oakland Research Institute	NDMS	National Disaster Medical System
CHTC	Certified Hematopoietic Transplant Coordinator	NEMO	N-locus Expectation-Maximization using Oligonucleotide typing data
CIBMTR®	Center for International Blood & Marrow Transplant Research	NGS	Next Generation Sequencing
CIT	CIBMTR Information Technology	NHLBI	National Heart Lung and Blood Institute
CLIA	Clinical Laboratory Improvement Amendment	NIH	National Institutes of Health
CMCR	Centers for Medical Countermeasures Against Radiation	NIMA	Non-Inherited Maternal Antigen
CME	Continuing Medical Education	NIMS	National Incident Management System
CMF	Community Matching Funds	NK	Natural Killer
CMV	Cytomegalovirus	NLE	National Level Exercise
CNV	Copy Number Variation	NMDP®	National Marrow Donor Program
COG	Children's Oncology Group	NRP	National Response Plan
CREG	Cross Reactive Groups	NST	Non-myeloablative Allogeneic Stem Cell Transplantation
CSS	Center Support Services	OCR/ICR	Optical Character Recognition/Intelligent Character Recognition
CT	Confirmatory Testing	OIT	Office of Information Technology
CTA	Clinical Trial Application	OMB	Office of Management and Budget

**QUARTER PROGRESS REPORT****Development of Medical Technology for Contingency Response to Marrow Toxic Agents****October 01, 2013 through December 31, 2013**

DC	Donor Center	ONR	Office of Naval Research
DHHS-ASPR	Department of Health and Human Service – Assistant Secretary Preparedness and Response	P2P	Peer-to-Peer
DIY	Do it yourself	PBMC	Peripheral Blood Mononuclear Cells
DKMS	Deutsche Knochenmarkspenderdatei	PBSC	Peripheral Blood Stem Cell
DMSO	Dimethylsulphoxide	PCR	Polymerase Chain Reaction
DoD	Department of Defense	PSA	Public Service Announcement
DNA	Deoxyribonucleic Acid	QC	Quality control
DR	Disaster Recovery	RCC	Renal Cell Carcinoma
D/R	Donor/Recipient	RCI BMT	Resource for Clinical Investigations in Blood and Marrow Transplantation
DSTU	Draft Standard for Trial Use	REAC/TS	Radiation Emergency Assistance Center/Training Site
EBMT	European Group for Blood and Marrow Transplantation	REST	Representational State Transfer
ED	Emergency Department	RFP	Request for Proposal
EDC	Electronic Data Capture	RFQ	Request for Quotation
EFI	European Federation of Immunogenetics	RG	Recruitment Group
EM	Expectation Maximization	RITN	Radiation Injury Treatment Network
EMDIS	European Marrow Donor Information System	SBT	Sequence Based Typing
ENS	Emergency Notification System	SCTOD	Stem Cell Therapeutics Outcome Database
ERSI	Environment Remote Sensing Institute	SG	Sample Group
FACT	Federation for the Accreditation of Cellular Therapy	SHF	Synthetic Haplotype Frequency
FBI	Federal Bureau of Investigation	SLCBB	St. Louis Cord Blood Bank
FDA	Food and Drug Administration	SLW	STAR Link® Web
FDR	Fund Drive Request	SSA	Search Strategy Advice
FLOCK	Flow Cytometry Analysis Component	SSO	Sequence Specific Oligonucleotides
FP	Filter Paper	SSP	Sequence Specific Primers
Fst	Fixation Index	SSOP	Sequence Specific Oligonucleotide Probes
GETS	Government Emergency Telecommunications Service	STAR®	Search, Tracking and Registry

**QUARTER PROGRESS REPORT****Development of Medical Technology for Contingency Response to Marrow Toxic Agents****October 01, 2013 through December 31, 2013**

GCSF	Granulocyte-Colony Stimulating Factor (also known as filgrastim)	SW	Buccal Swab
GIS	Geographic Information System	TC	Transplant Center
GS	General Services	TED	Transplant Essential Data
GTR	Genetic Testing Registry	TNC	Total Nucleated Cell
GvHD	Graft vs Host Disease	TP	Time Point
HCS®	HealthCare Standard	TSA	Transportation Security Agency
HCT	Hematopoietic Cell Transplantation	UCSF	University of California – San Francisco
HEPP	Hospital Emergency Preparedness Program	UI	User Interface
HHQ	Health History Questionnaire	UML	Unified Modeling Language
HHS	Health and Human Services	URD	Unrelated Donor
HIPAA	Health Insurance Portability and Accountability Act	WGA	Whole Genome Amplification
HIS	Hispanic	WMDA	World Marrow Donor Association
HLA	Human Leukocyte Antigen	WU	Work-up